



Application No. 10/695,744

Docket No.: 2121-0178P

AMENDMENTS TO THE CLAIMS

1. (Previously Presented). A method for prenatal diagnosis of foetal cells isolated from maternal blood, comprising the following steps:

- a) filtering a sample of pure or diluted maternal blood on a filter, which has a pore size of between 6 and 15 μm , whereby epithelial cells are retained onto said filter;
- b) analyzing the cells retained on the filter for the presence of at least one immunological or cytological marker, which is characteristic of trophoblastic and/or syncytiotrophoblastic cells, to identify trophoblastic and/or syncytiotrophoblastic cells; and individually collecting at least one cell, which has been identified as being a trophoblastic and/or syncytiotrophoblastic cell, whereby a single cell, which is presumed to be of foetal origin, or a collection of single cells, which are presumed to be of foetal origin, is obtained;
- c) lysing the single cell of step b), or a single cell of the collection obtained at step b), whereby the genome of this single cell is made accessible to amplification primers,
- d) amplifying the genome of the lysed single cell obtained at step c), whereby a pre-amplification product is obtained from a single cell,
- e) using the pre-amplification product obtained at step d), both to demonstrate the foetal origin of the single cell, and to carry out the prenatal diagnosis, wherein:
 - i. said pre-amplification product is analyzed for the presence of genetic or polymorphism marker(s), which can, or the allelotyping of which can, be distinguished from the one(s) of a maternal cell genome, by amplification of said marker(s) from said pre-amplification product, whereby said presence demonstrates the foetal origin of said single cell, and

ii. if said foetal origin is demonstrated, identifying at least one genetic or chromosomal anomaly of the foetus, or a genotype thereof, by genetic analysis of said pre-amplification product.

2. –3. (Cancelled).

4.(Previously Presented). The method of claim 1, wherein the cells retained on the filter are collected individually by microdissection.

5. (Previously Presented). The method of claim 4, wherein said microdissection consists of laser cutting the portion of the filter on which a cell is retained then recovering the single collected cell in a suitable tube.

6. – 8. (Cancelled).

9. (Previously Presented). The method of claim 1, wherein said identification of at least one genetic or chromosomal anomaly of the foetus, or of a genotype thereof, is carried out by identifying one or more genetic target(s) in said preamplification product.

10. (Previously Presented). The method of claim 1, wherein prior to step e), the preamplification product of step d) is purified to obtain a preparation of preamplified DNA derived from the genome of said single cell.

11. (Previously Presented). The method of claim 9, wherein said at least one genetic or chromosomal anomaly of the foetus, or said genotype thereof, is identified by amplification of one or more sequence(s) carrying the genetic target(s), from said preamplification product.

12. (Previously Presented). The method of claim 11, wherein said amplification of one or more sequence(s) carrying the genetic target(s) is carried out from less than one fifth of said preamplification product.

13. (Previously Presented). The method of claim 11, wherein said identification of at least one genetic or chromosomal anomaly of a foetus, or of said genotype thereof, is demonstrated by sequencing the genetic target(s) carried in the amplified sequence(s).

14. (Previously Presented). The method of claim 10, wherein said at least one genetic or chromosomal anomaly of the foetus, or said genotype thereof, is identified by hybridization of all or a portion of the preamplified DNA preparation with specific DNA probes or Peptide Nucleic Acid (PNA) type probes.

15. (Previously Presented). The method of claim 14, wherein the specific DNA probes are fixed on a support forming a DNA micro- or macro-array.

16. (Previously Presented). The method of claim 1 or 4 or 5 or any one of claims 9 to 15, wherein at least one of said polymorphism markers is a microsatellite marker, a Variable Number of Tandem Repeats (VNTR) marker, a Single Nucleotide Polymorphism (SNP) marker or a Short Tandem Repeat (STR) marker.

17. (Previously Presented). The method of claim 1, wherein the foetal origin is demonstrated by identifying a marker or a combination of markers, the presence of which, or the allelotyping of which, is specific to the DNA of paternal cells.

18. (Previously Presented). The method of claim 10, wherein a chromosomal anomaly is identified by a method for comparative genomic hybridization (CGH) of:

- said preamplified DNA preparation derived from the genome of said single cell, the foetal origin of which has been demonstrated, and of
- a preamplified DNA preparation of cells of maternal origin or of non foetal reference cells.

19. (Cancelled).

20. (Previously Presented). The method of claim 1, wherein the filtered maternal blood is derived from a blood sample made after the fifth week of pregnancy.

21. (Previously Presented). The method of claim 1, wherein said filtering of maternal blood is a filtering of 1 to 10 mL of maternal blood.

22. (Previously Presented). The method of claim 1, wherein the maternal blood sample is diluted 10 to 100 fold in a filtration solution.

23. (Previously Presented). The method of claim 1, wherein the pure or diluted maternal blood sample is filtered using a filter, the pores, of which have a diameter of about 8 μm .

24. (Previously Presented). The method of claim 23, wherein the filter has pores with a diameter of about 8 μm and a pore density in the range 5×10^4 to 5×10^5 pores/cm².

25. (Previously Presented). The method of claim 1, wherein the filter is a polycarbonate filtration membrane, and all of the pores of said polycarbonate filtration membrane have a substantially identical diameter.

26. – 29. (Cancelled).